UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,462	05/01/2001	Jehad Charo	1430-264	7394

7590 07/16/2002

Nixon & Vanderhye
1100 North Glebe Road 8th Floor
Arlington, VA 22201-4714

EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	11

DATE MAILED: 07/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/763,462	CHARO ET AL.	
	Examiner	Art Unit	
	C. Qian	1636	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *14-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 May 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-24 are pending in the application.

This office action is in response to the Amendment filed on 4/16/02.

Response to Amendment

Acknowledgment is made of Applicants' submission of a substitute specification on 4/12/02; therefore, the objection to the specification has been withdrawn.

The lack of unity requirement is maintained and made final for reasons discussed in the Office Action mailed on 1/16/02 and further discussed below.

The rejection of claims 8 and 10 under 35 U.S.C. 112, first paragraph has been withdrawn in light of Applicants' arguments.

The rejection of claim 5 under 35 U.S.C. 112, second paragraph is maintained for reasons of record set forth in the Office Action mailed on 1/16/02 and as further discussed below.

The rejection of claims 1, 7-9 and 11-13 under 35 U.S.C 103 is maintained for reasons of record set forth in the Office Action mailed on 1/16/02 and further discussed below.

Claims 2-4, 10 and 24 are rejected under 35 U.S.C. 103 (a) as set forth below.

Claims 2-4, 6 and 11 are rejected under 35 U.S.C. 112, second paragraph as set forth below.

Response to Arguments

In response to the lack of unity requirement set forth in the previous office actions, Applicants argue that this application is subject to lack of unity practice instead of restriction practice under 35 U.S.C. 371. Applicants further argue that the claims do form single general inventive concept under PCT Rule 13.1. Applicants also argue that the compounds recited in

claim 1 are Schiff base compounds, however, Applicants imply that selection of one species from the group is a distinct invention.

The examiner agrees that the current application is a national stage of PCT EP99/06217 which does not subject it to restriction practice. However, the lack of unity requirement under **37 C.F.R. 1.475 (Unity of Invention before the International Searching Authority, the International Preliminary Examining Authority and during the national stage)** clearly applies to the instant application. Although the subtitle on page 2 of the previous office action is Restriction/Election, the content of the section clearly indicates that the Lack of Unity practice is applied. Therefore, for the same reasons set forth in the prior office action (1/16/02), the lack of unity requirement is maintained and only the claims directed to elected subject matter (1-13 and 24) are under examination on merits currently. The examiner acknowledges that Applicants did not make a statement that the selection of one species of Schiff base forming compound is not a distinct invention, however, if Applicants regard each compound can constitute a distinct invention from the other, the unity of invention would have been broken. Applicants are advised to clarify this matter. Currently, all the compounds listed in claim 1 are under examination.

In response to the rejection of claim 5 under 35 U.S.C. 112, second paragraph, Applicants argue that the term "substantially simultaneous" is definite because the specification discloses that the term means "preferably at the same time, or if not, at least within a few hours either side of DNA sequence administration." This is not deemed persuasive because it is not clear how many hours apart would have been to administer the compound before or after the DNA administration. Therefore, this rejection is maintained.

In response to the rejection of claims 1, 7-9 and 11-13 under 35 U.S.C. 103 (a), Applicants argue that 1) Rhodes (US 5,508,310) excludes tucaresol from the disclosure; 2) tucaresol is disclosed as a traditional vaccine adjuvant in WO 94/07479, which does not have reasonable expectation of success as an adjuvant in DNA vaccine; 3) Herrmann et al. does not provide additional motivation to Rhodes because this reference teaches that adjuvant, a substance has the ability of promoting DNA uptake or recruiting immune system cells to the site of inoculation, which is different from the agents that would "enhance both humoral and cellular immune responses initiated by the antigenic peptide" as required by the claims of the present invention.

The above arguments have been considered and deemed not persuasive. Although Rhodes excludes tucaresol in the invention that is drawn to the use of Schiff base forming compound for the manufacture of a medicament for the potentiation of an immune response, Rhodes does not exclude tucaresol as a Schiff base forming compound and an immunopotentiator. In fact, Rhodes demonstrates that tucaresol increased T-lymphocyte priming to antigen (see Figure 1 and col. 14, lines 33-37); therefore, Rhodes teaches tucaresol as an immunopotentiator and an effective vaccine adjuvant.

Contrary to Applicants' assertion that DNA vaccines use different mechanisms than those of "traditional" vaccines to achieve their effect in the body, it is the antigenic peptide encoded by the nucleic acid that elicits immune response rather than the nucleic acid itself. The antigenic peptide produced using cell's machinery is no different from the antigenic peptide broken down from the killed or subunit vaccine. In addition, Rhodes teaches that the mechanism for the immunopotentiating action of the Schiff base forming compound such as tucaresol is that it

reacts with amino groups on the surface of lymphocytes and antigen presenting cells, thus provides costimulation to T-cells, and amplifying the costimulation provided by physiological Schiff base-formation between antigen and amino groups on the surface of lymphocytes. Therefore, there is sufficient motivation and reasonable expectation of success for using a Schiff base forming compound as DNA vaccine adjuvant because it would amplify the costimulation between antigenic peptides and lymphocytes.

The prior office action does not state that Herrmann et al. provides additional motivation to Rhodes for using Schiff base forming compound as DNA vaccine adjuvant. As such, Applicants' arguments with regard to this reference are not deemed persuasive.

Therefore, for the reasons made of record in the prior office action and discussed above, the invention would have been prima facie obvious to one of ordinary skill of art at the time the invention was made.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

Claims 2-4 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rhodes (US 5,508,310), in view of Herrmann et al (US 5,620,896).

The claims are drawn to a method of vaccinating a mammal comprising administering a nucleic acid encoding an antigenic peptide, and a Schiff base forming compound, wherein the administering of the compound is between one to seven occasions, between 14 days prior or post nucleic acid administration, between 7 days prior or post nucleic acid administration or between 24 hours prior of post nucleic acid administration. The claims are further drawn to a

combination of components comprising the nucleic acid encoding an antigenic peptide and a Schiff base-forming compound.

Rhodes (US 5,508,310) teaches Schiff base-forming compound can be used as vaccine adjuvant, and a vaccine can be prepared by formulating the antigenic component with said compound (see col.9, lines 38-42). Rhodes further discloses that the compound can be administered by oral, parenteral and inhalation at a dose range from 0.5 to 50mg/kg per day (see column 9, 7th-9th paragraph). Rhodes further teaches that the desired dose for the compound may be presented as between two to four sub-doses administered at appropriate intervals throughout the day (see col.9, lines 59-61), simultaneously administered with the antigen and/or additional injections following antigen administration (see col.14, lines 16-20). Rhodes also teaches that the Schiff base compounds may be administered to the patient by oral, parenteral (including subcutaneous, intradermal, intramuscular and intravenous), rectal, nasal (in forms of powder, for example) and pulmonary routes (see col.9, lines 43-46, and col.10, lines 65 through col.11, lines 1-47). However, Rhodes does not teach the administration of a nucleic acid encoding an antigenic peptide in combination with a Schiff base compound or a combination of components comprising the nucleic acid and a Schiff base compound. Rhodes also does not teach a method of delivering the compound via gene gun.

Herrmann et al. (US 5,620,896) teaches a method of immunizing mammals against rotavirus infections by injecting a vector comprising DNA encoding antigenic peptide to the mammals in the presence of adjuvant (see column 7, 2nd–4th paragraph).

Combining the teaching of Rhodes and Herrmann et al., it would have been obvious to one of ordinary skill in the art to practice the method of vaccinating a mammal by administering

a nucleotide encoding an antigenic peptide, and augmenting immune response of said vaccine by combining a Schiff base compound as adjuvant using the dosing schedule taught by Rhodes. The ordinary artisan would have been motivated to use Schiff base compound as a vaccine adjuvant because of the teaching of Rhodes, who not only teach those compounds can stimulate immune response but also provides the mechanism of such stimulation. The ordinary artisan would have a reasonable expectation of success because of the teaching of Herrmann et al., who teach a method of vaccinating a mammal by administering a vector comprising DNA encoding an antigenic peptide with an adjuvant, and the teaching of Rhodes, who teaches that Schiff base compound can potentiate immune response at the dosing schedule mentioned above. The ordinary artisan would also have been motivated to combine a nucleic acid encoding a antigenic peptide with a Schiff base compound to make a formulation of vaccine. Therefore, the invention is obvious to one of ordinary skill in the art at the time the invention is made.

Claim 10 rejected under 35 U.S.C. 103(a) as being unpatentable over Rhodes, in view of Hermman et al. and Bellhouse et al. (US 5,630,796).

Bellhouse et al. teach a device (gene gun) that provides effect transdermal delivery of therapeutic agents. Bellhouse et al. teach that the device (gene gun) delivers the particle form of a therapeutic agent, preferably powdered form, by generating a supersonic gas flow in which the therapeutic agent is injected (see col.1, lines 35-44, also Figure 1). Bellhouse et al. further teach an example of successful delivery of insulin to rats (see col.9, example 1). In addition, Bellhouse et al. teach that this delivery method is quicker and safer to use than liquid drug by syringe and needle, and no sharps to dispose afterwards (see col.1, lines 62-65).

It would have been obvious to one of ordinary skill of art to vaccinating a mammal with a nucleic acid encoding an antigenic peptide and a Schiff base compound to enhance the immunity generated by said antigenic peptide for reasons discussed in the prior office action and above. It would have been obvious to one of ordinary skill of art to deliver the Schiff base compound using the device taught by Bellhouse et al. The ordinary artisan would have been motivated to do so because the advantages of the needleless injection taught by Bellhouse et al (see col.1, 62-65). The ordinary artisan would have reasonable expectation of success because the teaching of Rhodes, who teaches that Schiff base compounds can be formulated in powder form, and the teaching of Bellhouse et al., who teach a device (gene gun) and a method of delivering therapeutic agents in powder form to a mammal. Therefore, the invention would have been prima facie obvious to one of ordinary skill of art at the time the invention was made.

Claim Rejections - 35 USC § 112

Claims 2-4, 6 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 6, the recitation of "which is repeated..." renders the claim indefinite because it is unclear whether the nucleic acid administration, the Schiff base compound administration or a combination of both is repeated.

Regarding claims 2-4, 6 and 11, the word "about" renders the claims indefinite because the boundary or limitation set forth by claims is unclear. For example, is 16 days prior to the administration of nucleic acid falls within the limit set by claim 2?

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
July 15, 2002

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600